

TENT COOPERATION TRE

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D AMERIQUE

in its capacity as elected Office

Date of mailing (day month year) 12 April 2000 (12.04.00)	
International application No PCT GB99 02761	Applicant's or agent's file reference MEDW P21404PC
International filing date (day month year) 19 August 1999 (19.08.99)	Priority date (day month year) 27 August 1998 (27.08.98)
Applicant COHEN, Patricia, Townsend, Wade et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

16 March 2000 (16.03.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

S. Mafla

Form PCT/B/401 (3.7.1992)

Translation of Form PCT/B/401 (3.7.1992)

Doc. No. 1/97

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MEDW/P21404PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as where applicable, item 5 below	
International application No. PCT/GB 99/ 02761	International filing date (day/month/year) 19/08/1999	(Earliest) Priority Date (day/month/year) 27/08/1998
Applicant MEDICAL RESEARCH COUNCIL et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II)

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

PROTEIN DOMAINS IN THE HEPATIC GLYCOGEN-TARGETTING SUBUNIT OF PROTEIN PHOSPHATASE 1 AND METHODS OF MAKING AND USING THE SAME ✓

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 1-5 and 13-15 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 12
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 12

Present claim 12 and claims 13 and 14, as far as they relate to claim 12, relate to a compound and method defined (inter alia) by the ability to compete with peptide PEWPSYLGYEKLYPPY in a test method.

The use of the test method in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is impossible to compare the parameters the applicant has chosen to employ with what is set out in the prior art. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, no search has been performed for the above mentioned compounds and methods.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Int. Application No.
PCT/GB 99/02761

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/47 A61K38/17 G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	C.G. ARMSTRONG ET AL.: "Identification of the separate domains in the hepatic glycogen-targeting subunit of protein phosphatase 1 that interact with phosphorylase a, glycogen and protein phosphatase 1" BIOCHEMICAL JOURNAL, vol. 336, 15 December 1998 (1998-12-15), pages 699-704, XP002127680 page 702, left-hand column, paragraph 4 -page 703, right-hand column, paragraph 2; figure 7 ----- -/-	1-5, 13, 14

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

14 January 2000

Date of mailing of the international search report

28/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Fuhr, C

INTERNATIONAL SEARCH REPORT

Int'l Application No.

PCT/GB 99/02761

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>G. MOORHEAD ET AL.: "Purification of the hepatic glycogen-associated form of protein phosphatase-1 by microcystin-Sepharose affinity chromatography" FEBS LETTERS, vol. 362, 1995, pages 101-105, XP002127681 AMSTERDAM NL page 101, left-hand column, paragraph 2 -right-hand column, paragraph 1 page 104, right-hand column, paragraph 1 -page 105, left-hand column, paragraph 1</p>	1
A	<p>J.L. MARTIN ET AL.: "Glucose Analogue Inhibitors of Glycogen Phosphorylase: The Design o Potential Drugs for Diabetes" BIOCHEMISTRY, vol. 30, 20 October 1991 (1991-10-20), pages 10101-10116, XP002122960 EASTON, PA US page 10112, right-hand column, paragraph 1 -page 10115, left-hand column, last paragraph</p>	1
A	<p>W.H. MARTIN ET AL.: "Discovery of a human liver glycogen phosphorylase inhibitor that lowers blood glucose in vivo" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 95, February 1998 (1998-02), pages 1776-1781, XP002122959 WASHINGTON US page 1779, right-hand column, paragraph 2 -page 1781, left-hand column, paragraph 1</p>	1
A	<p>EP 0 846 763 A (MEDICAL RES COUNCIL ;UNIV DUNDEE (GB); SMITHKLINE BEECHAM CORP (US) 10 June 1998 (1998-06-10) claims</p>	1

Form PCT/ISA 210 (patent family annex) (July 1992)

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
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DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

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REC'D 05 DEC 2000

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

5

Applicant's or agent's file reference MEDY/P21404PC		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
FOR FURTHER ACTION		
International application No. PCT/GB99/02761	International filing date (day/month/year) 19/08/1999	Priority date (day/month/year) 27/08/1998
International Patent Classification (IPC) or national classification and IPC C07K14/47		
Applicant MEDICAL RESEARCH COUNCIL et al.		



1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 16/03/2000	Date of completion of this report 30.11.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Renggli-Zulliger, N Telephone No. +49 89 2399 7482 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/02761

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-34 as originally filed

Claims, No.:

1-14 as originally filed

Drawings, sheets:

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/02761

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-6, 12-14.

because:

☒ the said international application, or the said claims Nos. 1-5, 13-14 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-3, 6, 13, 14 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 12, 13(partially) and 14(partially).

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/02761

Novelty (N)	Yes:	Claims	4, 5, 7-11
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	8
	No:	Claims	4, 5, 7, 9-11
Industrial applicability (IA)	Yes:	Claims	6-12
	No:	Claims	-

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I

Basis of this report

4. Additional observations :

The subject-matter of claims 4, 7 and 9 was examined based on the sequence disclosed in the description (pages 4-7) i.e. PEWPSYLGYEKLGPYY corresponding to the C-terminal 16 amino acids of rat liver G_L (page 4, lines 4-5) as disclosed in sequence ID n°3 of D2.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1) Claims 1-5, 13-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

2) No opinion with regard to novelty, inventive step and industrial applicability was established on the subject-matter of claims 1-3, 6, 13, 14 because of lack of clarity.

The compound as characterised in the claim can be an infinite number of very different substances that are not necessarily structurally related, rendering subject-matter of claims 1-3, 6, 13-14 not clearly defined. So many chemical compounds or polypeptides can fall under the scope of the claim that no meaningful interpretation with respect to novelty and inventive step can be made.

Furthermore, the particular parameters used to define the above mentioned compound have not been tested for drugs or peptides of the prior art. Consequently, this renders impossible to evaluate whether or not these products fall under the scope of the claims.

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: G. MOORHEAD ET AL.: 'Purification of the hepatic glycogen-associated form of protein phosphatase-1 by microcystin-Sepharose affinity chromatography' FEBS LETTERS, vol. 362, 1995, pages 101-105.

D2: EP-A-0 846 763 (MEDICAL RES COUNCIL ;UNIV DUNDEE (GB); SMITHKLINE BEECHAM CORP (US), 10 June 1998.

Novelty (Article 33(1) and (2) PCT)

1) The medical use or a pharmaceutical composition comprising the 16mer amino acid sequence of PEWPSYLGYEKLGPYY or a method for identifying an inhibitor compound using this 16mer amino acid sequence are not disclosed in the cited prior art. Therefore, the subject-matter of claims 4, 5, 7, 8-11 is novel.

Inventive step (Article 33(1) and (3) PCT)

1) Document D1 which is considered to be the closest prior art, discloses the cloning of liver G_L and its binding to *phosphorylase a* (Figure 5).

The difference between D1 and the present application is the provision of a inhibitor of the above mentioned interaction to be used in medicine.

In view of D1, the problem to be solved is to provide an inhibitor of the binding of *phosphorylase a* and G_L to be used in medicine.

The solution proposed by the present application is to use a polypeptide comprising the sequence PEWPSYLGYEKLGPYY in medicine in order to block the interaction of *phosphorylase a* and G_L.

The question to be answered with respect to inventive step is whether it was obvious for the person skilled in the art to use a polypeptide comprising that sequence to block the binding of *phosphorylase a* and G_L .

From D1, it is clear that G_L binds to *phosphorylase a* and the sequence of G_L is known from D2 (Sequence ID n°3). Therefore, the use of one of the partner of the binding, such as the full-length G_L to inhibit/compete with that binding is part of the obvious strategies used by the person skilled in the art.

Moreover, the medical use of such an inhibitor is evident due to the biochemical role that PP1 enzyme plays in the glycogen metabolism, including modulation of glycogen synthase as developed in D2 (page 2, lines 14-38, 57-58 and page 3, lines 1-2).

Therefore, as far as the full-length of G_L is concerned, the subject-matter of claims 4, 5 and 7 does not involve an inventive step in view of D1 in combination with D2 and the common general knowledge.

2) Methods to identify potential inhibitors of a known binding using the full-length proteins is well known in the art as illustrated in D2 (page 3, lines 47-58). Therefore, in view of D1 in combination with D2 and the common general knowledge, the subject-matter of claims 9-11 does not involve an inventive step.

3) The subject-matter of claim 8 appears to be inventive, because it cannot be derived from the cited prior art that a truncated version of the glycogen-targeting subunit of protein phosphatase 1 can be able to block the interaction of G_L with protein phosphatase 1, since the identification of the particular domains involved in that interaction are not known. However, the attention of the applicant is drawn to the fact that this claim is dependent on claim 6 for which no opinion could be formulated with regard to novelty, inventive step (see RE Item III of this IPER).

Industrial application (Article 33(1) and (4) PCT)

4) For the assessment of the present claims 1-5, 13-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known com-

pound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII**Certain observations on the international application**

- 1) Claims 1 and 6 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not defined. The claim attempts to define the subject-matter in terms of the result to be achieved which merely amounts to a statement of the underlying problem. Such a definition is only allowable under the conditions elaborated in the PCT Guidelines, Section IV, III, 4.7. In this instance, however, such a formulation is not allowable, because it appears possible to define the subject-matter in more concrete terms, as for example, by including structural features such as a part of the sequence of the claimed protein.
- 2) Subject-matter of claims 1 and 6 is broader than what is disclosed in the present application in which only one peptide (page 4, lines 4-5) is disclosed but no other example that could allow such a generalisation. Therefore subject-matter of claim 1 is not supported by the description in its full breadth as required by Article 6 PCT, as its scope is broader than justified by the description and the figures. Technical features such as the nucleotide or an amino acid sequences should be included.
- 3) The term "fragment" used in claims 4, 7 and 9 is not clear in the sense of Article 6 PCT, because the size of such fragments is not defined rendering the limits of the claims undefined too.
- 4) The term "variants" in claims 4, 7 and 9 is not clear in the sense of Article 6 PCT, since the extent of such variations is not precised. This term could comprise not even functionally related sequences that share very little homology to the reference sequence. The description does not seem to be enabling for such a broad subject-matter.